



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/941,945	08/30/2001	Brigitte Bathe	032301WD190	6360

7590 07/27/2004
SMITH, GAMBRELL & RUSSELL, LLP
SUITE 800
1850 M STREET, N.W.
WASHINGTON, DC 20036

EXAMINER

KERR, KATHLEEN M

ART UNIT	PAPER NUMBER
----------	--------------

1652

DATE MAILED: 07/27/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/941,945	BATHE ET AL.	
	Examiner	Art Unit	
	Kathleen M Kerr	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 May 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 12,14,16,19,23-25 and 29-35 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 12,14,16,19,24 and 25 is/are allowed.
- 6) ☒ Claim(s) 23 and 29-35 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
- ☒ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input checked="" type="checkbox"/> Other: <u>alignment</u> . |

DETAILED ACTION

Application Status

1. In response to the previous Office action, a non-final rejection (mailed on February 23, 2004), Applicants filed a response and amendment received on May 24, 2004. Said amendment amended Claims 12, 19, 23, 24, 29-31, 33, and 35. Thus, Claims 12, 14, 16, 19, 23-25, and 29-35 are pending in the instant Office action and will be examined herein.

Priority

2. As previously noted, the instant application is granted the benefit of priority for the foreign application 10043331.6 filed in Germany on September 2, 2000. Receipt is acknowledged of papers submitted under 35 U.S.C. § 119(a)-(d), which papers have been placed of record in the file. Said papers are not in English; no translation has been filed.

Contrary to the Examiner's previous assertion that the SEQ ID NO:1 in the instant application did not match SEQ ID NO:1 in the foreign priority document, said sequences do, indeed, match as evidenced by visual inspection of the Examiner prompted by Applicant's assertion that they do match. The error appears to be in the "Geneseq" database used by the Examiner in searching and not in the original priority document.

Despite the matching of SEQ ID NO:1 in the instant application to the sequence listing in the foreign priority document, said document cannot be used to grant an earlier effective filing date because no English translation has been provided as required. However, no outstanding art rejections rely on this earlier date so the point of an earliest effective filing date is moot.

Art Unit: 1652

In summary, the Examiner confirms that the instant application is granted foreign priority to DE 100 43 331.6 filed on September 2, 2000 and that DE 100 43 331.6 discloses SEQ ID NO:1 exactly. However, the earliest effective filing date for the instant claims is the filing date of August 30, 2001 (instant application) due to the absence of an English translation of the priority document. No translation is required since no outstanding art rejections need be overcome.

Withdrawn - Objections to the Specification

3. Previous objection to the specification for being confusing concerning the phrase on page 6, paragraph [0024], “enzyme sigma factor D” is withdrawn. Applicant argues that the filing of P10726 (Nice Prot View) in an IDS confirms that enzyme sigma factor D is, indeed, well known in the art. The Examiner agrees in part, now that document referred to as “submitted herewith” in Applicant’s previous remarks (filed 11/17/03 in page 4) has been clarified as being P10726. While the Examiner maintains that sigma factor D is not an enzyme (nor does P10726 purport sigma factor D to be an enzyme), this issue has now been clarified on the record that “enzyme sigma factor D”, as noted in the specification, is intended to mean “RNA polymerase sigma-D factor” as described in P10726. The objection is herein withdrawn.

Withdrawn - Claim Objections

4. Previous rejection of Claim 29 under 37 C.F.R. § 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim is withdrawn by virtue of Applicant’s amendment rewriting Claim 29 in independent form.

Art Unit: 1652

Withdrawn - Claim Rejections - 35 U.S.C. § 112, second paragraph

5. Previous rejection of Claims 23 and 24 under 35 U.S.C. § 112, second paragraph, as being indefinite for the various gene names is withdrawn, in part, by virtue of Applicant's amendment deleting said gene names from the claims. Moreover, proteins "a protein for lysine export" and "a Zwa2 protein" have been removed from the claims.

Maintained - Claim Rejections - 35 U.S.C. § 112, second paragraph

6. Previous rejection of Claim 23 under 35 U.S.C. § 112, second paragraph, as being indefinite is maintained, in part, by virtue of the retention of "Zwa1 protein" in Claim 23. Applicant's arguments have been fully considered but are not deemed persuasive for the following reasons.

Applicant argues that the zwa1 protein is well known in the art by virtue of its disclosure in USPN 6,632,644. The Examiner disagrees. USPN 6,632,644 teaches a single example of what the inventors name as zwa1, said example being from *C. glutamicum*. No genus is described in the patent so that one of skill in the art would be able to recognize such as genus, as required for the language of instant Claim 23. No function of the species of zwa1 that is disclosed in USPN 6,632,644 so that one of skill in the art might be able to glean characteristics of such a genus from the disclosure. Thus, the nature of a gene encoding any zwa1 protein, as required for the genus in Claim 23, is unclear.

Withdrawn - Claim Rejections - 35 U.S.C. § 112, first paragraph

7. Previous rejection of Claim 23 under 35 U.S.C. § 112, first paragraph, written description, is withdrawn by virtue of Applicant's amendment removing reference to the

Art Unit: 1652

subgenus of “feedback resistant” enzymes (as opposed to the genera of any aspartate kinase or threonine dehydratase).

8. Previous rejection of Claims 23-24 under 35 U.S.C. § 112, first paragraph, written description, is withdrawn, in part, by virtue of Applicant’s amendment removing optional limitations of “a protein for lysine export” and “a Zwa2 protein”.

9. Previous rejection of Claim 23 under 35 U.S.C. § 112, first paragraph, scope of enablement, is withdrawn by virtue of Applicant’s removal of feedback-resistance aspartate kinases and threonine dehydratases from the claim.

10. Previous rejection of Claims 23-24 under 35 U.S.C. § 112, first paragraph, scope of enablement, because the specification, while being enabling for methods using known *zwa1*, *zwa2*, and *lysC* genes as described in the specification, does not reasonably provide enablement for methods using other of these genes, is withdrawn in part by virtue of Applicant’s amendment removing optional limitations of “a protein for lysine export” and “a Zwa2 protein”.

11. Previous rejection of Claims 12, 14, 16, 19, 23-25, 29-35 under 35 U.S.C. § 112, first paragraph, scope of enablement, because the specification, while being enabling for overexpressing SEQ ID NO:1 by transforming a host cell with a vector comprising SEQ ID NO:1 and a promoter, does not reasonably provide enablement for overexpressing SEQ ID NO:1 by means otherwise mentioned in the specification, is withdrawn by virtue of Applicant’s amendment limiting said claims to overexpression via increased copy number and/or promoter usage as suggested by the Examiner.

Art Unit: 1652

Maintained - Claim Rejections - 35 U.S.C. § 112, first paragraph

12. Previous rejection of Claim 23 under 35 U.S.C. § 112, first paragraph, written description, is maintained, in part, with respect to “a Zwa1 protein”. Applicant’s arguments have been fully considered but are not deemed persuasive for the following reasons.

Applicant argues that the zwa1 protein is adequately described by virtue of its disclosure in DE 19959328.0, which document is incorporated by reference. The Examiner disagrees.

While said document adequately describes a species of zwa1 protein, that is the zwa1 protein from *C. glutamicum*, it is inadequate to support the genus, as claimed. Specifically for Claim 23 the Examiner previously noted the contrast of using named enzymes as follows:

“While genes encoding known enzymes with particular functions, such as genes encoding dihydrodipicolinate synthase, are adequately described by virtue of their specification function and their examples in the art, this is not the case for genes encoding proteins without clear support in the art for their genus: ... Zwa1 protein.... The mere name of these proteins does NOT connote a structure and/or function as is the case with the specific enzymes noted elsewhere in the claims. One example of each is noted in the specification; however, no description of how to maintain Zwa1-like protein structure and/or function is found. Thus, one of skill in the art would be unable to predict the structure of other members of the genus of genes claimed.”

For these reasons, description of a single example of a zwa1 gene does not adequately support the claimed genus.

13. Previous rejection of Claim 23 under 35 U.S.C. § 112, first paragraph, scope of enablement, because the specification, while being enabling for methods using known zwa1 genes as described in the specification, does not reasonably provide enablement for methods using other of these genes, is maintained. Applicant’s arguments have been fully considered but are not deemed persuasive for the following reasons.

Art Unit: 1652

Applicant argues that previous remarks with respect to clarity and written description obviate the enablement rejection with respect to the *zwa1* gene. The Examiner disagrees for the reasons noted above in disagreement of Applicant's arguments against the rejections under 35 U.S.C. § 112, second paragraph, as well as 35 U.S.C. § 112, first paragraph, written description.

NEW ISSUES

Claim Objections

14. Claim 23 is objected to for having improper language. In line 11, "a gene which encodes a aspartate kinase" (emphasis added) is improper. The language should be ---an aspartate kinase--- or remove the ---a--- altogether. Correction is required.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

15. Claim 29 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The combination of "consisting of" and "comprising" is confusing with respect to the polynucleotide to be overexpressed. The Examiner suggests changing "consisting of" to ---comprising--- for clarity. Correction is required.

16. Claim 30 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as

Art Unit: 1652

the invention. In the claim, item a requires only that bacteria comprise the sigD gene and produce amino acids; thus, the wherein clause about overexpression is confusing since overexpression is not mentioned previously in the claim. Clarification is required. For purposes of examination, this claim will be interpreted as requiring transformation of a vector comprising SEQ ID NO:1 to meet all the limitations of the claim.

Claim Rejections - 35 U.S.C. § 103

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

17. Claims 29 and 31-35 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Nakagawa *et al.* (EP 1108790). The instant claims are drawn to methods of making and isolating L-amino acids by culturing *C. glutamicum* transformed with a polynucleotide encoding SEQ ID NO:2 or with SEQ ID NO:1 from 301-864.

Nakagawa *et al.* (EP 1108790) teach methods of making amino acid using transformants comprising SEQ ID NO:669 (see page 4, item 15), which sequence is identical to SEQ ID NO:1 from 301-864 (see attached alignment) and which exactly encoded SEQ ID NO:2. Nakagawa *et al.* (EP 1108790) do not expressly teach using *C. glutamicum* in said methods.

Nakagawa *et al.* (EP 1108790) further teach that *C. glutamicum* is useful in the production of amino acids (see page 2, paragraphs 2 and 3).

Art Unit: 1652

At the time of the invention, it would have been obvious to one of ordinary skill in the art to use *C. glutamicum* as the transformant in the methods expressly taught by Nakagawa *et al.* (EP 1108790) because *C. glutamicum* are well-known amino acid producers and Nakagawa *et al.* (EP 1108790) teach this fact. One would have been motivated to combine the teachings found in Nakagawa *et al.* (EP 1108790) because amino acid production is commercially profitable (see page 2, paragraph 3).

18. Claims 29 and 31-35 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Nakagawa *et al.* (USPAP 2002/0197605). The instant claims are drawn to subject matter as noted above. The reasoning for the instant rejection is identical to that noted above; USPAP 2002/0197605 is a U.S. filing of EP 1108790.

Summary of Issues Pending

19. The following is a summary of the issues pending in the instant application:

- a) Claim 23 stands objected to for having improper language.
- b) Claim 23 stands rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for the retention of “Zwa1 protein”.
- c) Claim 29 stands rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for the combination of “consisting of” and “comprising” language.
- d) Claim 30 stands rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for the confusing wherein clause about overexpression.
- e) Claim 23 stands rejected under 35 U.S.C. § 112, first paragraph, written description, for “a Zwa1 protein”.
- f) Claim 23 stands rejected under 35 U.S.C. § 112, first paragraph, scope of enablement, because the specification, while being enabling for methods using known *zwa1* genes as described in the specification, does not reasonably provide enablement for methods using other of these genes.
- g) Claims 29 and 31-35 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Nakagawa *et al.* (EP 1108790).
- h) Claims 29 and 31-35 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Nakagawa *et al.* (USPAP 2002/0197605).

Examiner's Comments

20. The Examiner had previously noted that Applicants “have not overexpressed the sigD gene, SEQ ID NO:1, encoding a 188 amino acid protein (SEQ ID NO:2), in coryneform to produce L-lysine in culture.” As noted by Applicants, this is contrary to a statement made on page 10 of the specification which states: “In the course of work carried out in connection with the present invention it was established that coryneform bacteria after overexpression of the sigD gene produce amino acids in an improved manner.” No particulars of overexpression means, level of improvement, or any experimental specifics are noted. Therefore, while the Examiner redacts the generalized statement as requested by Applicant, the lack of data and experimental specifics is herein noted.

Despite this lack of specifics in the specification, “the Examiner has no evidence to indicate that overexpression of sigD will abolish the lysine production already in coryneform. No requirement that overexpression of sigD *increases* amino acid production in coryneform need be met for the pending claims. Thus, the claims are enabled for such methods, which methods have utility since amino acids are important nutritional additives” (from previous Office action).

Nakagawa *et al.* (EP 1108790) disclose the entire genome of *C. glutamicum*. Nakagawa *et al.* teach the full-length of SEQ ID NO:1 as embedded in their sequences 7060 and 7061 (genomic sequences), but Nakagawa *et al.* do not teach using these entire genome sequence to produce amino acids (which would be a species of Claim 1 herein since said claim has open language with respect to the polynucleotide sequence), nor is such a method obvious despite the disclosure of the full sequence in a single SEQ ID NO. Thus, Claims 12, 14, 16, 19, 23-25, and 30 are free of the prior art. The Examiner also notes a related JP document as JP 2002/191370.

Conclusion

21. Claims 12, 14, 16, 19, 24, and 25 are allowed in the Office action; claims 23 and 29-35 are rejected for the reasons identified in the numbered sections of this Office action. Applicants must respond to the objections/rejections in each of the numbered sections in this Office action to be fully responsive in prosecution.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See M.P.E.P. § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. § 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kathleen M Kerr whose telephone number is (571) 272-0931. The examiner can normally be reached on Monday through Friday, from 9:00am to 6pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathupura Achutamurthy can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

A handwritten signature in black ink, appearing to read 'Kathleen M Kerr', is positioned above the printed name.

Kathleen M Kerr
Examiner
Art Unit 1652

July 21, 2004

ALIGNMENT

LOCUS AX120753 564 bp DNA linear PAT 11-MAY-2001
 DEFINITION Sequence 669 from Patent EP1108790.
 ACCESSION AX120753
 VERSION AX120753.1 GI:14037468
 SOURCE Corynebacterium glutamicum
 ORGANISM Corynebacterium glutamicum
 Bacteria; Actinobacteria; Actinobacteridae; Actinomycetales;
 Corynebacterineae; Corynebacteriaceae; Corynebacterium.
 REFERENCE 1
 AUTHORS Nakagawa,S., Mizoguchi,H., Ando,S., Hayashi,M., Ochiai,K.,
 Yokoi,H., Tateishi,N., Senoh,A., Ikeda,M. and Ozaki,A.
 TITLE Novel polynucleotides
 JOURNAL Patent: EP 1108790-A 669 20-JUN-2001;

Query Match 50.0%; Score 564; DB 6; Length 564;
 Best Local Similarity 100.0%; Pred. No. 1.5e-147;
 Matches 564; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy	301	TTGGCTGATACTGAGCGCGAGCTCGCTGACCTGGTACCGCAGGCAACGGCGGGCGATCGT	360
Db	1	TTGGCTGATACTGAGCGCGAGCTCGCTGACCTGGTACCGCAGGCAACGGCGGGCGATCGT	60
Qy	361	CGGGCATTGCAAAGAATAATGGAGATTATTCACCCCATTTGTTTTCGCTTATGCTCGCGCT	420
Db	61	CGGGCATTGCAAAGAATAATGGAGATTATTCACCCCATTTGTTTTCGCTTATGCTCGCGCT	120
Qy	421	CGTATTGGAGGTGGACGCCAGCCAACGGCAGAAGACGTTGCTCAAGAAATCTGCCTGGCG	480
Db	121	CGTATTGGAGGTGGACGCCAGCCAACGGCAGAAGACGTTGCTCAAGAAATCTGCCTGGCG	180
Qy	481	GTAGCCACCTCCATTAGGAACTTTGTCGACCAGGGTAGGCCGTTTCATGGCGTTTGTCTAC	540
Db	181	GTAGCCACCTCCATTAGGAACTTTGTCGACCAGGGTAGGCCGTTTCATGGCGTTTGTCTAC	240
Qy	541	GGCATTGCATCTAACAAGGTCGCAGATGCTCACAGGGCGATGTCGAGGGATAAATCGACT	600
Db	241	GGCATTGCATCTAACAAGGTCGCAGATGCTCACAGGGCGATGTCGAGGGATAAATCGACT	300
Qy	601	CCTATTGAGGAAGTCCCAGAACTTCACCAGATACTTTTACCCCCGAAGACTTTGCGCTG	660
Db	301	CCTATTGAGGAAGTCCCAGAACTTCACCAGATACTTTTACCCCCGAAGACTTTGCGCTG	360
Qy	661	GTCAGCGATGGAAGTAACAGAGTTAGGGAAGTTCTCGATCTACTGAGTGAAAAGGCACGC	720
Db	361	GTCAGCGATGGAAGTAACAGAGTTAGGGAAGTTCTCGATCTACTGAGTGAAAAGGCACGC	420
Qy	721	GACATTCTTATCTTGAGAGTTATCGTTGGTCTTTCCGCAGAAGAACTGCAGAGATGGTG	780
Db	421	GACATTCTTATCTTGAGAGTTATCGTTGGTCTTTCCGCAGAAGAACTGCAGAGATGGTG	480
Qy	781	GGCAGCACCCCAGGTGCTGTACGAGTTGCCCAACACAGGGCACTCACGACACTTCGAAGC	840
Db	481	GGCAGCACCCCAGGTGCTGTACGAGTTGCCCAACACAGGGCACTCACGACACTTCGAAGC	540
Qy	841	ACACTTGAGCAGCAGGAGAACAAG	864
Db	541	ACACTTGAGCAGCAGGAGAACAAG	564